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Reproductive Hormones and Implication of Synthetic Hormonal Preparations: Current Status

Atiya Asim and Somia Gul*

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jinnah University for Women, Pakistan

***Corresponding author:** Somia Gul, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jinnah University for Women, 74600, Karachi, Pakistan

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Abbreviations: FSH: Follicle-Stimulating Hormone; LH: Luteinizing Hormone; hCG: Human Chorionic Gonadotropin Hormone; GnRH: Gonadotropin Releasing Hormone; r-hFSH: Recombinant Follicular Stimulating Hormone; HRT: Hormonal Replacement Therapy; ERT: Estrogen-Replaced Therapy; MGA: Melengestrol; ART: Assisted Reproductive Technologies

ABSTRACT

Objective of this study is to evaluate data on synthetic preparations of reproductive hormones and provides a broad view of their usage and new approaches in research and development in terms of implication of synthetic hormonal preparations, benefitting many aspects of life other than reproduction. The evolution of the steroid hormones provides a brilliant competition in research, major advances in the field of medicine and better outcomes in terms of marketed products. Extensive literature search has been carried out on reproductive hormones and implication of synthetic hormonal preparations. Current studies reveal the comprehensive details of different applications of synthetically prepared hormonal preparations in the fields of reproduction, infertility, cosmetics, food production, cancer, neurological dysfunctions and transgender hormone replacement therapy. The development in the field of synthetic production of reproductive hormones has open a door for variety of its application in numerous aspects of life. New approaches in the implication of synthetic steroidal hormones include treatment of stroke, traumatic brain and spinal cord injuries, as well as in satisfying gender dysphoria, and hormonal implants has been used to enhance growth, feed intake and reproductive efficiency in animals to satisfy the increasing demand of food supply.

Keywords: Reproductive Hormones; Synthetic Hormonal Preparations; Infertility; Hormonal Implants

Introduction

A woman of 24yrs old had no problem in conceiving just after married but she couldn't maintain her pregnancy due to unknown reasons. After 11 weeks of pregnancy, she had started spotting which leads to miscarriage. In second pregnancy she experienced a same threat of abortion and doctor prescribed her Gravibinan inj (hydroxyprogesterone) 4 times weekly along with Duphaston (Dydrogesterone) tablet once in a day for 1 month and advised her for taking bed rest which leads to a successful pregnancy. Advancement in science of medicine creates more chances for a woman to reproduce. Reproductive hormones are usually produced in the ovaries (females) and in testes (males) and these hormones are responsible to control reproductive cycles [1]. Estrogen and Progesterone are considered as main female sex hormones and Testosterone as main male hormone [2]. Other reproductive hormones include follicle-stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin hormone (hCG), gonadotropin releasing hormone (GnRH), Oxytocin [3]. Some of these hormones can be synthetically prepared now for use in various aspects [4]. Before the development in the synthetic production of reproductive hormones, there were many complexities in reproduction like difficulty in conceiving, stability of pregnancy, complexities at the time of birth and others but now it has minimized due to advancement in the field of hormonal therapy [5].

Infertility can be explained as not having pregnancy after 1yr of trying and it may be related to either one of the partners or other combination of factors that resist pregnancy [6]. Follicle stimulating hormone (FSH) is a reproductive hormone, glycoprotein in nature, produced in several isoforms by anterior pituitary gland are used in assisted reproductive technologies (ART) [7]. Recombinant follicular stimulating hormone (r-hFSH) has widely been used in the treatment of infertility [8]. If the infertility in man is due to gonadotropin deficiency, then gonadotropin replacement therapy is highly effective in producing spermatogenesis and fertility [9]. *In vitro* fertilization (IVF) is a process to overcome infertility in women, in this process a woman's egg is taken and fused with a sperm in a lab setting and a fertilized egg is implant back into a woman's uterus to make her pregnant [10]. Long-acting gonadotropin releasing hormone (GnRH) analogues has been giving to woman, who is willing for a baby through IVF process, before ovarian stimulation results in better outcomes of treatment by increasing the number and quality of oocytes recovered and by decreasing the rate of cycle cancellation [11]. Stability of pregnancy has now become most common issue, less than 30% of women experience threatened abortion, it is the most serious problem in the first trimester of pregnancy, in order to support pregnancy and avoid threat of abortion different therapies given to pregnant woman including hormonal therapy like human chorionic gonadotropin (hCG) or 17-α-hydroxyprogesterone. Treatment with hCG has more better outcomes than with hydroxyprogesterone [12]. Unconstrained preterm labor leads to more than half of preterm birth which is a cause of neonatal morbidity and mortality [13]. A hormone derivative called hydroxyprogesterone caproate is available in injection form, used to reduce the risk of recurrent pre-term delivery in high risk patients [14]. Buserelin is a synthetic analogue of GnRH which is an agonist at pituitary GnRH receptors [15]. The GnRH agonist buserelin be regarded as a development in the treatment of a variety of gynaecological, andrological, paediatric and oncological conditions, infertility and other reproductive hormone dependent conditions, with a low chances of adverse treatment effects [16]. Menopause or stopping of menstrual cycle in women brings a lot of effects on an individual including their skin. Women can avoid side effects of menopause by taking hormonal replacement therapy (HRT) along with estrogen-replaced therapy (ERT) with an appropriate cosmetology [17]. Estrogen and progesterone were previously considered as primary hormones in controlling reproductive cycles in females, are now being researched as protective and regenerative agents in neurological dysfunctions like stroke, traumatic brain and spinal cord injuries [18].

Hypogonadism in men is a clinical syndrome results from either unable to produce desired level of testosterone in a body or to produce normal amount of sperm or both [19]. Testosterone therapy is used to treat this deficiency and has found no unfavourable risks in healthy young men [20]. Hormonal implants has been used by researchers to enhance growth, feed intake and reproductive efficiency in animals to satisfy the increasing demand of food supply [21]. Melengestrol (MGA) is available as a food additive for growth enhancement but approved only for used in beef heifers [22]. Estradiol benzoate along with progesterone used for manipulating estrus cycle and ovulation in ruminants [23,24], estradiol benzoate either used alone or along with progesterone, testosterone propionate, or trenbolone acetate used in implant formulations for beef cattle production [25]. Although these methods are useful in providing sufficient food supply to humans but in the recent studies we have observed that as the consumption of milk, meat and egg increased in the last few years we have also observed decreases in semen quality [26], increase in the chances of cryptorchidism, hypospadias and some cancers associated with hormones which includes testicular, breast, prostate and endometrial cancers [27]. Gonadotropins have been extensively studied for their function in maintaining balance between cell proliferation and differentiation, and therefore in cancer [28,29] (Table 1).

Table 1: Marketed reproductive hormones and their uses.

Reproductive Hormone	Synthetic Derivatives of Reproductive Hormones	Dosage Forms Available	Use in Different Fields
Follicle stimulating hormones (FSH)	Recombinant follicular stimulating hormone (rFSH)	Injection	Used for infertility in women
Gonadotropin	Gonadotropin-releasing hormone analogue. Human chorionic gonadotropin(hCG)	Injection	In-vitro fertilization, cancer, male infertility, stability of pregnancy
Progesterone	17α-hydroxyprogesterone. Hydroxyprogesterone caproate Progesterone Melengestrol (MGA)	Injection, Vaginal pessaries, capsules.	Stability of pregnancy Reduce Pre-term labor Neurological dysfunction, Manuplating estrus cycle in ruminants. Food additive for growth production of beef heifer.

Estrogen	Estrogen Estradiol benzoate	Injection, Gel, Tablet.	Transgender dysphoria, Neurological dysfunction, Cosmetology. Manipulating estrus cycle in ruminants. Formulations for beef cattle production.
Testosterone	Testosterone Testosterone propionate	Tablet, Capsules, Injection.	Hypogonadism Formulations for beef cattle production.

Breast cancer is most common in women, tamoxifen is a selective estrogen receptor modulator used as a standard of care in treating breast cancer but gonadotropin releasing hormone analogues (GnRHa) used as an additional treatment option by suppressing ovarian function [30]. Transgenders, whose deep-seated belief differs from the sex they were assigned at the time of their birth [31]. Medical help as well as surgeries for changing gender like male to female or female to male are practicing now days. Hormonal therapy plays a role of backbone in terms of medical help for patients undergoing gender transition [32]. Most of transgender women encounter gender dissatisfaction and to line up with a more feminine gender role they take estrogen [33] and anti-androgen therapy to reduce body and facial hair, decreased muscle mass, increase in breast size and fat distribution [34]. As we know that sex steroids induce some changes in breast tissue during hormonal therapy taken by transwomen, therefore it has been found that there is an increased risk of breast cancer in those transwomen who received hormonal treatment [35,36]. There are many aspects of synthetic reproductive hormones other than its effect on human reproductive system; researchers are finding new implementations of them in future. One of those future researches involve finding ways to treat male infertility without harming women as until now women has to face all the circumstances of assisted reproductive technologies (ART) even in cases where female is normal but infertility factor is due to male [37].

Conclusion

The increasing demand of hormonal therapy found by researchers were once considered for the reproductive purposes only but now it has been implicated in achieving artificial fertilization. New approaches in the implication of synthetic steroidal hormones include treatment of stroke, traumatic brain and spinal cord injuries, as well as in satisfying gender dysphoria and hormonal implants has been used to enhance growth, feed intake and reproductive efficiency in animals to satisfy the increasing demand of food supply.

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